



I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail, in an envelope addressed to: Commissioner for Patents, P. O. Box 1450, Alexandria, VA, 22313-1450 on the date shown below.

Dated: Signature: (Eileen Sheffield)

Docket No.: NY-HUBR 1189-US  
(10104500)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:  
Peter Sondermann, et al

Application No.: 09/856,933

Group Art Unit: 1644

Filed: February 27, 2002

Examiner: M. A. Belyavskyi

For: RECOMBINANT SOLUBLE Fc RECEPTEORS

Commissioner for Patents  
P. O. Box 1450  
Alexandria, Va. 22313-1450

DECLARATION

The UNDERSIGNED hereby declares as follows:

1. I am one of the correctly named co-inventors of the referenced application, and am fully familiar with the application and its prosecution.  
*or participated in it* *24th January 2005* *16*
2. I have conducted experiments that demonstrate that pharmaceutical compositions containing a recombinant soluble Fc<sub>Y</sub>R<sub>IIb</sub> receptor, wherin the receptor contains the amino acid sequence of SEQ ID NO: 3, can be used to treat autoimmune diseases, allergies or tumor diseases.
3. DBA/1 mice with experimental allergic encephalomyelitis (EAE) are an accepted animal model for multiple sclerosis (MS). EAE is induced in the mice by immunization with myelin oligodendrocyte glycoprotein (MOG), which results in MS-like symptoms (e.g., paralytic symptoms, brain lesions). Thirty DBA/1 mice were immunized with MOG to induce EAE and were then treated (in groups of ten) at 48 hour intervals with either PBS (control 1), 100 µg trp-synthase from *E. coli* (control 2) or 100 µg soluble Fc<sub>Y</sub>R<sub>IIb</sub> receptor. Symptoms of EAE were individually evaluated and the disease index was calculated for each mouse in accordance with Abdul-Majid, et al., *J. Neuroimmunol.* 111:23-33 (2000). The disease index was considerably lower when Fc<sub>Y</sub>R<sub>IIb</sub> was administered as compared to both controls.
4. NZBW/F<sub>1</sub> mice represent an accepted animal model for systemic lupus erythematosus (SLE) (See Theofilopoulos and Dixon, *Adv. Immunol.* 37: 269-390 (1985)). Groups of ten NZBW/F<sub>1</sub> mice each were treated subcutaneously with either PBS (control group) or 100 µg soluble Fc<sub>Y</sub>R<sub>IIb</sub> receptor at weekly intervals. The results showed that the survival rate was considerably increased by administering Fc<sub>Y</sub>R<sub>IIb</sub> compared to the control. After

40 weeks, all mice treated with Fc $\gamma$ Rllb were alive. However, 70% of the control group had died after this time period.

5. An important criterion in analyzing progression of SLE is proteinuria of the diseased NZBW/F<sub>1</sub> mice, which occurs as a result of developing glomerulonephritis. The proteinuria of the mice treated as described in 4, *supra*, was determined. The results indicate that administration of Fc $\gamma$ Rllb considerably slowed the increase in proteinuria as compared to the control group.
6. An accepted animal model for rheumatoid arthritis is adjuvant-induced arthritis (AIA) in mice. The inflammatory reaction is caused by administering an antigen into a joint. Treatment of these mice was carried out by administering either 100  $\mu$ g soluble Fc $\gamma$ Rllb receptor or a control, intraperitoneally at weekly intervals in accordance with Waksman, *J. Immunol.* 166(1): 12-34 (2002) and Holmdahl, et al., *Immunol. Rev.* 184: 184-202 (2001). The arthritis index was calculated as [joint diameter of arthritic knee joint (mm) divided by joint diameter of contralateral knee joint (mm)] multiplied by 100. Administration of Fc $\gamma$ Rllb significantly decreased the arthritis index in the mice as compared to the control.
7. Immune complex (IC) -induced alveolitis in mice represents an accepted animal model for inflammatory diseases that are associated with a high immune complex burden. In order to induce the disease, mice were injected intraperitoneally with an antigen and intratracheally with an antibody directed against the antigen. This caused the formation of immune complexes in the lung that result in inflammatory reactions. Hemorrhaging and the infiltration of neutrophils (PMN) were evaluated. 100  $\mu$ g Fc $\gamma$ Rllb was simultaneously administered intraperitoneally in accordance with Tanoue, et al., *Int. Arch. Allergy Immunol.* 101(1): 47-51 (1993) and Yoshizawa, et al., *Clin. Immunol. Immunopathol.* 61(3): 376-386 (1991). Administration of Fc $\gamma$ Rllb almost completely suppressed the inflammatory reactions and also reduced hemorrhage.
8. The results of these experiments show that Fc $\gamma$ Rllb, containing the amino acid sequence of SEQ ID NO: 3, has a clear positive effect on the course of diseases in which immune complexes are involved, in particular autoimmune diseases.
9. I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information or belief are believed to be true; and further that these statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements and the like so made may jeopardize the validity of this declaration, the subject application, or any patent issued thereon.

Dated:

24/01/05

By Uwe /   
Dr. Uwe Jacob